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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/403,440	01/19/2000	DAVID PHILIP LANE	39749-0001APC	7276

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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	
MAIL DATE	**DELIVERY MODE**
05/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/403,440	LANE, DAVID PHILIP	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, 8 are being examined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 8 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Bottger et al, 1996 (Oncogene, 13: 2141-2147), in view of McCann A H et al, 1995 (British J Cancer, 71(5): 981-5), and further in view of Lee JM et al, 1995 (Cancer and metastasis Review, 14(2): 149-161) for reasons already of record in paper of 09/11/07.

In the response of 03/11/08, a Declaration of Professor Karen Vousden was submitted.

The response asserts that the Examiner clearly errs in interpreting McCann et al. to teach that MDM2 tumors are significantly associated with tumors having low levels of p53 staining. The response asserts that McCann et al. teach that tumours with high MDM2 expression are associated with low p53 and this is only 7% of the cancers. The response asserts that although some of the data, especially in Table Ill, might be conceivably interpreted to indicate that even tumors that express lower amounts of MDM2 are associated with low p53 levels, one might be reluctant to drawn conclusions from data that the authors have chosen not to highlight themselves.

The response asserts that even if one assumes that the results of McCann et al. indicate that MDM2 expression (either type 1 or type 2) is correlated with low p53, this is not sufficient basis for a conclusion that tumors that do not overexpress MDM2 are also associated with low p53 levels.

The submission of the Declaration by Professor Karen Vousden is acknowledged.

The response has been considered but is not found to be persuasive for the following reasons:

Type 1 breast cancer has low expression of MDM2, and most of which (12 over a total of 14) also has negative or low expression of p53 ("low" is less than 10% found on cancer cells, as defined by McCann et al, abstract, line 8) (McCann et al, table III on page 983). Thus similar to type 2 (MDM+) breast cancer, the presence of MDM2 is associated with low level of p53. Since there is no clear definition of "not overexpressed" in the specification, one would have reasonably interpreted that low level of MDM2 is not overexpression of MDM2. One would have expected that in said type 1 breast cancer, in which there is association between the presence of MDM2 and absence or low of expression of p53, MDM2 would bind to and inhibit the function of p53, similar to the situation in which MDM2 is higher expressed (type 2, MDM2+ in more than 10% of cancer cells) and the level of p53 is low (McCann et al, abstract), in view of the teaching of Bottger et al that MDM2 is a natural inhibitor of p53 (p.2141, fist column).

One would have motivated to treat type 1 breast cancer patients, to enhance the expression of p53, in view of the teaching of Bottger et al that MDM2 binds to and inhibits the

function of p53, and further in view of the teaching of Lee et al that loss of p53 function is correlated with resistance to chemotherpeutic agent.

The response asserts that McCann et al. did not include a normal tissue control in their experiment, and thus it is not clear what normal expression is. The response asserts that the fact that most of the tumors are negative for MDM2 staining does not mean that such tumors do not express MDM2, only that it is below the level of detection in that particular assay. The response asserts that as a result, this part of the data is hard to interpret, which might be a reason why the authors have chosen to base their conclusions on the tumors that clearly over-express MDM2 (the type 2 staining ones).

The response asserts that McCann et al. teach that most breast cancers arise without evidence for amplification or overexpression of MDM2. and that such cancers are not associated with low levels of p53. The response asserts that absent comparative normal tissue data in the McCann et al. paper, it is unknown what MDM2 overexpression is. The response asserts that it is most likely that both type 2 and type 1 tumors are actually overexpressing MDM2, and the tumors with negative expression are those without overexpression. The response asserts that using this interpretation of the McCann et al. data, even if type 1 tumors are taken into account (which the authors did not), it would still be clear that most breast cancers arise without evidence of MDM2 overexpression or amplification, and these tumors are not associated with low levels of p53 (34/74 of them have type 2 and 3 p53 staining). The response concludes that thus, in the 40 tumors without MDM2 staining and with low levels of p53 there must be another mechanism to inactivate p53, and that inhibiting the p53/MDM2 interaction would not necessarily work in such cases.

The response has been considered but is not found to be persuasive for the following reasons:

The interpretation of type 1 breast cancer, as the type of breast cancer, in which MDM2 is not overexressed, has been set forth above.

Concerning the expression of MDM2 in normal tissue, it is not germane here, because the issue is: 1) the relative expression of MDM2 and p53 in four different types of breast cancer patients, which ranges from negative, low (less than 10%), to (10%-50%) and more than 50% positive, and 2) the association of MDM2 and p53 expression in different types of breast cancer patients.

Concerning 40 negative type breast cancer patients, which have no detectable MDM2 and no detectable or low level of p53 (Table I-II), or in 34 negative type breast cancer patients, which have no detectable MDM2 but high expression of p53 (Type 2 or 3 expression of p53) (Table II), since MDM2 is not present, a correlation between MDM2 and p53 cannot be determined. Thus, negative breast cancer patients would not be considered or applied by the combined art.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply

is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
May 20, 2008

/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643